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=> dis his nofile

     (FILE 'HOME' ENTERED AT 15:51:29 ON 16 AUG 2007)

     FILE 'REGISTRY' ENTERED AT 15:51:38 ON 16 AUG 2007
L1              STR
L*** DEL2241598 S L
L2            5 SEA SSS SAM L1
L3          115 SEA SSS FUL L1

=> d l3 que stat;fil medl,biosis,embase,caplus;s l3
L1              STR
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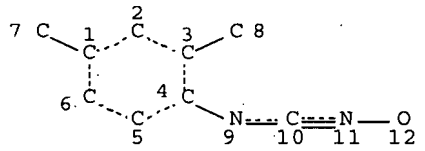


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
L3          115 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED     187 ITERATIONS                          115 ANSWERS
SEARCH TIME: 00.00.01


FILE 'MEDLINE' ENTERED AT 15:53:18 ON 16 AUG 2007

FILE 'BIOSIS' ENTERED AT 15:53:18 ON 16 AUG 2007
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FILE 'CAPLUS' ENTERED AT 15:53:18 ON 16 AUG 2007
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L4            0 FILE MEDLINE
L5           23 FILE BIOSIS
L6            0 FILE EMBASE
L7           41 FILE CAPLUS

TOTAL FOR ALL FILES
L8           64 L3

=> s cerebr? vascul? disease or stroke or cerebrovasospasm or blood(5a)subarachnoid
or head injur?
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L9       115250 FILE MEDLINE
L10       92093 FILE BIOSIS
L11      125191 FILE EMBASE
L12       37304 FILE CAPLUS

TOTAL FOR ALL FILES
L13      369838 CEREBR? VASCUL? DISEASE OR STROKE OR CEREBROVASOSPASM OR BLOOD(5
                A) SUBARACHNOID OR HEAD INJUR?

=> s l8 and l13
L14           0 FILE MEDLINE
L15           1 FILE BIOSIS
L16           0 FILE EMBASE
L17           3 FILE CAPLUS

TOTAL FOR ALL FILES
L18           4 L8 AND L13

=> dup rem l18
PROCESSING COMPLETED FOR L18
L19           3 DUP REM L18 (1 DUPLICATE REMOVED)

=> d 1-3 ibib abs hitstr

L19  ANSWER 1 OF 3  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
     DUPLICATE 1
ACCESSION NUMBER:    2007:36889  BIOSIS  Full-text
DOCUMENT NUMBER:     PREV200700029005
TITLE:               Protective effect of the 20-HETE inhibitor HET0016 on brain
                     damage after temporary focal ischemia.
AUTHOR(S):           Poloyac, Samuel M. [Reprint Author]; Zhang, Yuqing; Bies,
                     Robert R.; Kochanek, Patrick M.; Graham, Steven H.
CORPORATE SOURCE:    Univ Pittsburgh, Sch Pharm, Dept Pharmaceut Sci, 808A Salk
                     Hall, Pittsburgh, PA 15261 USA
                     poloyac@pitt.edu
SOURCE:              Journal of Cerebral Blood Flow & Metabolism, (DEC 2006)
                     Vol. 26, No. 12, pp. 1551-1561.
                     CODEN: JCBMDN. ISSN: 0271-678X.
DOCUMENT TYPE:       Article
LANGUAGE:            English
ENTRY DATE:          Entered STN: 27 Dec 2006
                     Last Updated on STN: 27 Dec 2006
AB   Cytochrome P450 metabolism of arachidonic acid produces the potent
     vasoconstrictive metabolite, 20-hydroxyeicosatetraenoic acid (20-HETE). Recent
     studies have implicated 20-HETE as a vasoconstrictive mediator in hemorrhagic
     stroke. The purpose of this study was to determine the effect of the 20-HETE
     inhibitor, HET0016, on lesion volume and cerebral blood flow (CBF) after
     temporary middle cerebral artery occlusion (MCAO) in rats. Plasma
     pharmacokinetics and tissue concentrations of HET0016 were determined after a
     10 mg/kg intraperitoneal dose. Separate rats were treated with HET0016 or
     vehicle before 90 mins of MCAO. Lesion volume was assessed by 2,3,5-
     triphenyl-tetrazolium-chloride and cerebral flow was determined using laser
     Doppler flow. The effect of MCAO on in vitro microsomal formation of mono-
     oxygenated arachidonic acid metabolites was also determined. Results show
     that HET0016 has a short biologic half-life, distributes into the brain, and
     is associated with a 79.6% reduction in 20-HETE concentration in the cortex.
     Lesion volume was greatly reduced in HET0016-treated (9.1%+/- 4.9%) versus
     vehicle-treated (57.4%+/- 9.8%; n=6; P < 0.001) rats. An attenuation of the
     observed decrease in CBF was observed in HET0016-treated (180 mins 89.2%+/-
     6.2%; 240 mins 88.1%+/- 5.7% of baseline flow) versus vehicle control (180
```

mins 57.6%+/- 09.0%; 240 mins 53.8%+/- 20.0% of baseline flow; n=6; P < 0.05). Brain cortical microsomal formation rate of 20-HETE was also reduced at 24 dh in the ipsilateral hemisphere after MCAO. These data support a significant role for 20-HETE in the pathogenesis of ischemic stroke.

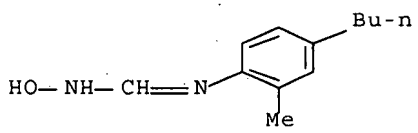
L19 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:353270 CAPLUS Full-text
DOCUMENT NUMBER: 136:363861
TITLE: Use of 20-HETE synthesizing enzyme inhibitors as therapy for cerebral vascular diseases
INVENTOR(S): Roman, Richard J.; Harder, David R.; Miyata, Noriyuki; Sato, Masakazu; Kameo, Kazuya; Okuyama, Shigeru
PATENT ASSIGNEE(S): MCW Research Foundation, Inc., USA; Taisho Pharmaceutical Co., Ltd.
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002036108	A2	20020510	WO 2001-US27605		20010906
WO 2002036108	A3	20021017			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2427557	A1	20020510	CA 2001-2427557		20010906
AU 200188798	A	20020515	AU 2001-88798		20010906
EP 1330240	A2	20030730	EP 2001-968558		20010906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004512361	T	20040422	JP 2002-538920		20010906
US 2005153871	A1	20050714	US 2001-937946		20010906
CN 1655775	A	20050817	CN 2001-818397		20010906
PRIORITY APPLN. INFO.:			US 2000-245638P	P	20001103
			WO 2001-US27605	W	20010906

AB A method for treating cerebral vascular diseases in a human or non-human animal is disclosed. The method involves inhibiting 20-HETE synthesizing enzyme activity sufficiently to increase or prevent a decrease in cerebral blood flow in the human or non-human animal.

IT 339068-25-6, HET0016
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of 20-HETE synthesizing enzyme inhibitors as therapy for cerebral vascular diseases by increasing cerebral blood flow)

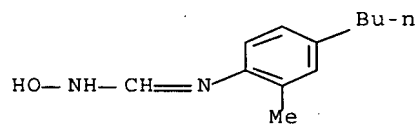
RN 339068-25-6 CAPLUS
CN Methanimidamide, N-(4-butyl-2-methylphenyl)-N'-hydroxy- (CA INDEX NAME)



L19 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:283486 CAPLUS Full-text
DOCUMENT NUMBER: 137:31503
TITLE: 20-HETE contributes to the acute fall in cerebral blood flow after subarachnoid hemorrhage in the rat
AUTHOR(S): Kehl, Franz; Cambj-Sapunar, Liana; Maier, Kristopher G.; Miyata, Noriyuki; Kametani, Shunishi; Okamoto, Hirotsugu; Hudetz, Anthony G.; Schulte, Marie L.; Zagorac, Drazen; Harder, David R.; Roman, Richard J.
CORPORATE SOURCE: Department of Physiology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA
SOURCE: American Journal of Physiology (2002), 282(4, Pt. 2), H1556-H1565
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study examined the effects of blocking the formation of 20-hydroxyeicosatetraenoic acid (20-HETE) on the acute fall in cerebral blood flow after subarachnoid hemorrhage (SAH) in the rat. In vehicle-treated rats, regional cerebral blood flow (rCBF) measured with laser-Doppler flowmetry fell by 30% 10 min after the injection of 0.3 mL of arterial blood into the cisterna magna, and it remained at this level for 2 h. Pretreatment with inhibitors of the formation of 20-HETE, 17-octadecynoic acid (17-ODYA; 1.5 nmol intrathecally) and N-hydroxy-N'-(4-butyl-2-methylphenyl)formamidine (HET0016; 10 mg/kg iv), reduced the initial fall in rCBF by 40%, and rCBF fully recovered 1 h after induction of SAH. The concentration of 20-HETE in the cerebrospinal fluid rose from 12 ± 2 to 199 ± 17 ng/mL after SAH in vehicle-treated rats. 20-HETE levels averaged only 15 ± 11 and 39 ± 13 ng/mL in rats pretreated with 17-ODYA or HET0016, resp. HET0016 selectively inhibited the formation of 20-HETE in rat renal microsomes with an IC50 of <15 nM and human recombinant CYP4A11, CYP4F2, and CYP4F3 enzymes with an IC50 of 42, 125, and 100 nM, resp. These results indicate that 20-HETE contributes to the acute fall in rCBF after SAH in rats.

IT 339068-25-6, HET0016
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(20-HETE role in acute fall in cerebral blood flow after subarachnoid hemorrhage in the rat)
RN 339068-25-6 CAPLUS
CN Methanimidamide, N-(4-butyl-2-methylphenyl)-N'-hydroxy- (CA INDEX NAME)



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REFERENCE COUNT:          45     THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> fil reg

FILE 'REGISTRY' ENTERED AT 15:55:17 ON 16 AUG 2007
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DICTIONARY FILE UPDATES:  15 AUG 2007  HIGHEST RN 944769-12-4

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predicted properties as well as tags indicating availability of
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on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> e "n-hydroxy-n'-(4-butyl-2-methylphenyl)-formamidine"/cn
E1            1      N-HYDROXY-N'-(2-METHYLAMINOETHYL)-2,3-BUTANEDIIMINE/CN
E2            1      N-HYDROXY-N'-(3-(METHYLTHIO)PROPYL)-N-((TRANS-2-PHENYLCYCLOP
                     ROPYL)METHYL)UREA/CN
E3            0 --> N-HYDROXY-N'-(4-BUTYL-2-METHYLPHENYL)-FORMAMIDINE/CN
E4            1      N-HYDROXY-N'-(4-METHOXYPHENYL)BENZAMIDINE/CN
E5            1      N-HYDROXY-N'-(4-METHYLPHENYL)-4-NITROBENZENECARBOXIMIDAMIDE/
                     CN
E6            1      N-HYDROXY-N'-(4-METHYLPHENYL)GUANIDINE/CN
E7            1      N-HYDROXY-N'-(M-CHLOROBENZOYLAMINO)-2,5-CYCLOHEXADIENEDIIMIN
                     E/CN
E8            1      N-HYDROXY-N'-(M-METHOXYPHENYL)UREA/CN
E9            1      N-HYDROXY-N'-(M-METHYLPHENYL)UREA/CN
E10           1      N-HYDROXY-N'-(M-NITROPHENYL)UREA/CN
E11           1      N-HYDROXY-N'-(O-HYDROXYBENZOYLAMINO)-2,5-CYCLOHEXADIENEDIIMI
                     NE/CN
E12           1      N-HYDROXY-N'-(O-METHOXYPHENYL)UREA/CN

=> e het0016/cn 5
E1            1      HET ACID-NEOPENTYL GLYCOL POLYMER, SRU/CN
E2            1      HET ANHYDRIDE/CN
E3            0 --> HET0016/CN
E4            1      HETA-AMOXICILLIN/CN
E5            1      HETACAT/CN

=> fil medl,biosis,embase,caplus,wpids

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=> s "n-hydroxy-n'-(4-butyl-2-methylphenyl)-formamidine" or
hydroxy(l)butyl(l)methylphenyl(l)formamidine? or het0016
L20          31 FILE MEDLINE
L21          45 FILE BIOSIS
L22          31 FILE EMBASE
L23          28 FILE CAPLUS
L24           9 FILE WPIDS

TOTAL FOR ALL FILES
L25         144 "N-HYDROXY-N'-(4-BUTYL-2-METHYLPHENYL)-FORMAMIDINE" OR HYDROXY(L
                ) BUTYL(L) METHYLPHENYL(L) FORMAMIDINE? OR HET0016

=> s l25 and l13
L26           3 FILE MEDLINE
L27           3 FILE BIOSIS
L28           3 FILE EMBASE
L29           3 FILE CAPLUS
L30           1 FILE WPIDS

TOTAL FOR ALL FILES
L31          13 L25 AND L13

=> fil medl,biosis,embase,caplus

FILE 'MEDLINE' ENTERED AT 15:57:46 ON 16 AUG 2007

FILE 'BIOSIS' ENTERED AT 15:57:46 ON 16 AUG 2007
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=> s l31 not l18
L36           3 FILE MEDLINE
L37           2 FILE BIOSIS
L38           3 FILE EMBASE
L39           0 FILE CAPLUS

TOTAL FOR ALL FILES
L40           8 L31 NOT L18
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PROCESSING COMPLETED FOR L40
L41            4 DUP REM L40 (4 DUPLICATES REMOVED)

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L41 ANSWER 1 OF 4 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2006684608 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16570075
TITLE: Protective effect of the 20-HETE inhibitor HET0016 on brain damage after temporary focal ischemia.
AUTHOR: Poloyac Samuel M; Zhang Yuqing; Bies Robert R; Kochanek Patrick M; Graham Steven H
CORPORATE SOURCE: Department of Pharmaceutical Sciences, School of Pharmacy, University of Pittsburgh, Pittsburgh, Pennsylvania 15261, USA.. poloyac@pitt.edu
CONTRACT NUMBER: 1R01NS052315-01 (NINDS)
EB001975-06 (NIBIB)
SOURCE: Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism, (2006 Dec) Vol. 26, No. 12, pp. 1551-61. Electronic Publication: 2006-03-29.
Journal code: 8112566. ISSN: 0271-678X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200612
ENTRY DATE: Entered STN: 25 Nov 2006
Last Updated on STN: 29 Dec 2006
Entered Medline: 28 Dec 2006

AB Cytochrome P450 metabolism of arachidonic acid produces the potent vasoconstrictive metabolite, 20-hydroxyeicosatetraenoic acid (20-HETE). Recent studies have implicated 20-HETE as a vasoconstrictive mediator in hemorrhagic stroke. The purpose of this study was to determine the effect of the 20-HETE inhibitor, HET0016, on lesion volume and cerebral blood flow (CBF) after temporary middle cerebral artery occlusion (MCAO) in rats. Plasma pharmacokinetics and tissue concentrations of HET0016 were determined after a 10 mg/kg intraperitoneal dose. Separate rats were treated with HET0016 or vehicle before 90 mins of MCAO. Lesion volume was assessed by 2,3,5-triphenyl-tetrazolium-chloride and cerebral flow was determined using laser Doppler flow. The effect of MCAO on in vitro microsomal formation of mono-oxygenated arachidonic acid metabolites was also determined. Results show that HET0016 has a short biologic half-life, distributes into the brain, and is associated with a 79.6% reduction in 20-HETE concentration in the cortex. Lesion volume was greatly reduced in HET0016-treated (9.1%+/-4.9%) versus vehicle-treated (57.4%+/-9.8%; n=6; P<0.001) rats. An attenuation of the observed decrease in CBF was observed in HET0016-treated (180 mins 89.2%+/-6.2%; 240 mins 88.1%+/-5.7% of baseline flow) versus vehicle control (180 mins 57.6%+/-19.0%; 240 mins 53.8%+/-20.0% of baseline flow; n=6; P<0.05). Brain cortical microsomal formation rate of 20-HETE was also reduced at 24 h in the ipsilateral hemisphere after MCAO. These data support a significant role for 20-HETE in the pathogenesis of ischemic stroke.

L41 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003209741 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12677022
TITLE: Contribution of 5-hydroxytryptamine1B receptors and 20-hydroxyeiscosatetraenoic acid to fall in cerebral blood flow after subarachnoid hemorrhage.
AUTHOR: Cambj-Sapunar Liana; Yu Ming; Harder David R; Roman Richard J
CORPORATE SOURCE: Department of Physiology, Medical College of Wisconsin, 8701 Watertown Plank Rd, Milwaukee, WI 53226, USA.
SOURCE: Stroke; a journal of cerebral circulation, (2003 May) Vol. 34, No. 5, pp. 1269-75. Electronic Publication: 2003-04-03.
Journal code: 0235266. E-ISSN: 1524-4628.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 6 May 2003
Last Updated on STN: 1 Jul 2003
Entered Medline: 30 Jun 2003

AB BACKGROUND AND PURPOSE: This study examined the interaction between 5-hydroxytryptamine1B (5-HT1B) receptors and 20-hydroxyeiscosatetraenoic acid (20-HETE) in contributing to the acute fall in regional cerebral blood flow (rCBF) after subarachnoid hemorrhage (SAH) in rats. METHODS: The effects of intracisternal injection of 0.3 mL of arterial blood, artificial cerebrospinal fluid, and 5-HT on rCBF and the levels of 20-HETE and 5-HT in cerebrospinal fluid were measured in rats pretreated with vehicle, a 5-HT1B receptor antagonist (isamoltane hemifumarate), or an inhibitor of the synthesis of 20-HETE (HET0016). The effects of HET0016 and isamoltane on the vasoconstrictor response and changes in [Ca2+]i to 5-HT were also studied in middle cerebral arteries and vascular smooth muscle cells isolated from these vessels. RESULTS: 20-HETE and 5-HT levels in cerebrospinal fluid rose from 172+/-10 to 629+/-44 ng/mL and from 6+/-4 to 1163+/-200 nmol/mL, respectively, after SAH. rCBF fell by 30% 10 minutes after SAH, and it remained at this level for the next 2 hours. Blockade of 5-HT1B receptors prevented the sustained fall in rCBF seen after SAH. Intracisternal injection of 5-HT mimicked SAH by increasing 20-HETE levels in cerebrospinal fluid to 475+/-94 ng/mL and reducing rCBF by 30%. Blockade of the synthesis of 20-HETE with HET0016 prevented the fall in rCBF produced by 5-HT. Isamoltane and HET0016 reduced the vasoconstrictor response of isolated MCA to 5-HT by >60% and diminished the rise in [Ca2+]i produced by 5-HT in vascular smooth muscle cells isolated from these arteries. CONCLUSIONS: These results suggest that the release of 5-HT after SAH activates 5-HT1B receptors and the synthesis of 20-HETE and that 20-HETE contributes to the acute fall in rCBF by potentiating the vasoconstrictor response of cerebral vessels to 5-HT.

L41 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002161743 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11893593
TITLE: 20-HETE contributes to the acute fall in cerebral blood flow after subarachnoid hemorrhage in the rat.
AUTHOR: Kehl Franz; Cambj-Sapunar Liana; Maier Kristopher G; Miyata Noriyuki; Kametani Shunishi; Okamoto Hirotsugu; Hudetz Anthony G; Schulte Marie L; Zagorac Drazen; Harder David R; Roman Richard J
CORPORATE SOURCE: Department of Physiology, Medical College of Wisconsin, Milwaukee, Wisconsin 53226, USA.

CONTRACT NUMBER: GM-56398 (NIGMS)
HL-10407-01 (NHLBI)
HL-29587 (NHLBI)
HL-29662 (NHLBI)
HL-59996 (NHLBI)
SOURCE: American journal of physiology. Heart and circulatory physiology, (2002 Apr) Vol. 282, No. 4, pp. H1556-65. Journal code: 100901228. ISSN: 0363-6135.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 15 Mar 2002
Last Updated on STN: 10 May 2002
Entered Medline: 9 May 2002

AB This study examined the effects of blocking the formation of 20-hydroxyeicosatetraenoic acid (20-HETE) on the acute fall in cerebral blood flow after subarachnoid hemorrhage (SAH) in the rat. In vehicle-treated rats, regional cerebral blood flow (rCBF) measured with laser-Doppler flowmetry fell by 30% 10 min after the injection of 0.3 ml of arterial blood into the cisterna magna, and it remained at this level for 2 h. Pretreatment with inhibitors of the formation of 20-HETE, 17-octadecynoic acid (17-ODYA; 1.5 nmol intrathecally) and N-hydroxy-N'-(4-butyl-2-methylphenyl)formamidine (HET0016; 10 mg/kg iv), reduced the initial fall in rCBF by 40%, and rCBF fully recovered 1 h after induction of SAH. The concentration of 20-HETE in the cerebrospinal fluid rose from 12 +/- 2 to 199 +/- 17 ng/ml after SAH in vehicle-treated rats. 20-HETE levels averaged only 15 +/- 11 and 39 +/- 13 ng/ml in rats pretreated with 17-ODYA or HET0016, respectively. HET0016 selectively inhibited the formation of 20-HETE in rat renal microsomes with an IC(50) of <15 nM and human recombinant CYP4A11, CYP4F2, and CYP4F3 enzymes with an IC(50) of 42, 125, and 100 nM, respectively. These results indicate that 20-HETE contributes to the acute fall in rCBF after SAH in rats.

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ACCESSION NUMBER: 2002218815 EMBASE Full-text
TITLE: 20-HETE contributes to the acute fall in cerebral blood flow after subarachnoid hemorrhage in the rat.
AUTHOR: Kehl F.; Cambj-Sapunar L.; Maier K.G.; Miyata N.; Kametani S.; Okamoto H.; Hudetz A.G.; Schulte M.L.; Zagorac D.; Harder D.R.; Roman R.J.
CORPORATE SOURCE: R.J. Roman, Dept. of Physiology, Medical College of Wisconsin, 8701 Watertown Plank Rd., Milwaukee, WI 53226, United States. rroman@mcw.edu
SOURCE: American Journal of Physiology - Heart and Circulatory Physiology, (2002) Vol. 282, No. 4 51-4, pp. H1556-H1565. .
Refs: 45
ISSN: 0363-6135 CODEN: AJPPDI
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
008 Neurology and Neurosurgery
LANGUAGE: English

SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 8 Jul 2002
Last Updated on STN: 8 Jul 2002

AB This study examined the effects of blocking the formation of 20-hydroxyeicosatetraenoic acid (20-HETE) on the acute fall in cerebral blood flow after subarachnoid hemorrhage (SAH) in the rat. In vehicle-treated rats, regional cerebral blood flow (rCBF) measured with laser-Doppler flowmetry fell by 30% 10 min after the injection of 0.3 ml of arterial blood into the cisterna magna, and it remained at this level for 2 h. Pretreatment with inhibitors of the formation of 20-HETE, 17-octadecynoic acid (17-ODYA; 1.5 nmol intrathecally) and N-hydroxy-N'-(4-butyl-2-methylphenyl)formamidine (HET0016; 10 mg/kg iv), reduced the initial fall in rCBF by 40%, and rCBF fully recovered 1 h after induction of SAH. The concentration of 20-HETE in the cerebrospinal fluid rose from 12 ± 2 to 199 ± 17 ng/ml after SAH in vehicle-treated rats. 20-HETE levels averaged only 15 ± 11 and 39 ± 13 ng/ml in rats pretreated with 17-ODYA or HET0016, respectively. HET0016 selectively inhibited the formation of 20-HETE in rat renal microsomes with an IC(50) of <15 nM and human recombinant CYP4A11, CYP4F2, and CYP4F3 enzymes with an IC(50) of 42, 125, and 100 nM, respectively. These results indicate that 20-HETE contributes to the acute fall in rCBF after SAH in rats.

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=> s roman r?/au;s harder d?/au;s miyata n?/au;s sato m?/au;s kameo k?/au;s okuyama
s?/au
L42         474 FILE MEDLINE
L43         752 FILE BIOSIS
L44         491 FILE EMBASE
L45         544 FILE CAPLUS

TOTAL FOR ALL FILES
L46        2261 ROMAN R?/AU


L47         334 FILE MEDLINE
L48         596 FILE BIOSIS
L49         323 FILE EMBASE
L50         262 FILE CAPLUS

TOTAL FOR ALL FILES
L51        1515 HARDER D?/AU


L52         286 FILE MEDLINE
L53         354 FILE BIOSIS
L54         312 FILE EMBASE
L55         848 FILE CAPLUS

TOTAL FOR ALL FILES
L56        1800 MIYATA N?/AU


L57        5522 FILE MEDLINE
L58        6740 FILE BIOSIS
L59        4543 FILE EMBASE
L60       18124 FILE CAPLUS

TOTAL FOR ALL FILES
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L61       34929 SATO M?/AU


L62          28 FILE MEDLINE
L63          55 FILE BIOSIS
L64          28 FILE EMBASE
L65         131 FILE CAPLUS

TOTAL FOR ALL FILES
L66         242 KAMEO K?/AU


L67         390 FILE MEDLINE
L68         558 FILE BIOSIS
L69         345 FILE EMBASE
L70         649 FILE CAPLUS

TOTAL FOR ALL FILES
L71        1942 OKUYAMA S?/AU

=> s l46 and l51 and l56 and l61 and l66 and l71
L72           0 FILE MEDLINE
L73           0 FILE BIOSIS
L74           0 FILE EMBASE
L75           1 FILE CAPLUS

TOTAL FOR ALL FILES
L76           1 L46 AND L51 AND L56 AND L61 AND L66 AND L71

=> d ibib abs

L76  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2002:353270  CAPLUS  Full-text
DOCUMENT NUMBER:          136:363861
TITLE:                    Use of 20-HETE synthesizing enzyme inhibitors as
                          therapy for cerebral vascular diseases
INVENTOR(S):              Roman, Richard J.; Harder, David R.
                          ; Miyata, Noriyuki; Sato, Masakazu
                          ; Kameo, Kazuya; Okuyama, Shigeru
PATENT ASSIGNEE(S):       MCW Research Foundation, Inc., USA; Taisho
                          Pharmaceutical Co., Ltd.
SOURCE:                   PCT Int. Appl., 38 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2002036108         A2    20020510    WO 2001-US27605         20010906
     WO 2002036108         A3    20021017
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             US, UZ, VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
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            BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2427557          A1    20020510    CA 2001-2427557          20010906
     AU 200188798        A     20020515    AU 2001-88798            20010906
     EP 1330240          A2    20030730    EP 2001-968558           20010906
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004512361       T     20040422    JP 2002-538920           20010906
     US 2005153871       A1    20050714    US 2001-937946           20010906
     CN 1655775          A     20050817    CN 2001-818397           20010906
PRIORITY APPLN. INFO.:                      US 2000-245638P     P    20001103
                                            WO 2001-US27605     W    20010906
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AB A method for treating cerebral vascular diseases in a human or non-human animal is disclosed. The method involves inhibiting 20-HETE synthesizing enzyme activity sufficiently to increase or prevent a decrease in cerebral blood flow in the human or non-human animal.

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=> s (l46 or l51 or l56 or l61 or l66 or l71)
L77        6950 FILE MEDLINE
L78        8888 FILE BIOSIS
L79        5964 FILE EMBASE
L80       20447 FILE CAPLUS

TOTAL FOR ALL FILES
L81       42249 (L46 OR L51 OR L56 OR L61 OR L66 OR L71)

=> s (l3 or l25 or l13) and l81
L82          95 FILE MEDLINE
L83         108 FILE BIOSIS
L84          90 FILE EMBASE
L85          57 FILE CAPLUS

TOTAL FOR ALL FILES
L86         350 (L3 OR L25 OR L13) AND L81

=> s l86 not (l76 or l40 or l18)
L87          93 FILE MEDLINE
L88         106 FILE BIOSIS
L89          88 FILE EMBASE
L90          55 FILE CAPLUS

TOTAL FOR ALL FILES
L91         342 L86 NOT (L76 OR L40 OR L18)

=> dup rem l91
PROCESSING COMPLETED FOR L91
L92         186 DUP REM L91 (156 DUPLICATES REMOVED)

=> d 1 abs

L92  ANSWER 1 OF 186  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on
     STN
AB   Jeffs et. al identified a genetic locus on chromosome 5 that is linked to
     infarct size following MCAO in SHRSP rats.  Contained within this QTL are the
     cytochrome P-450 4A omega-hydroxylase genes which catalyze the formation of
     the vasoconstrictor 20-HETE from arachidonic acid (AA).  Our lab has
     previously shown a role for 20-HETE in the pathogenesis of both hemorrhagic
     and ischemic models of stroke.  The purpose of this study was to measure
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cerebral vascular 20-HETE formation and CYP4A expression in SHRSP rats compared to stroke-resistant WKY and SHR strains. 20-HETE formation was quantified using triple quadrupole liquid chromatography mass spectrometry (LC/MS/MS). CYP4A protein expression was analyzed by western blot. Results indicate 20-HETE formation is significantly elevated in SHRSP rats relative to WKY and SHR (WKY 0.2237 +/- 0.0309 pmol/min/mg protein, n=6; SHR 0.3027 +/- 0.0459, n=5; SHRSP 0.3854 +/- 0.0368, n=5). Western blot analysis indicates significant elevation of CYP4A protein expression in SHRSP rats compared to WKY rats. Upregulation of cerebral vascular CYP4A expression and 20-HETE formation may contribute to sensitivity to cerebral ischemia in SHRSP rats.

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=> s (l3 or l25) and l13 and l81
L93             2 FILE MEDLINE
L94             2 FILE BIOSIS
L95             2 FILE EMBASE
L96             2 FILE CAPLUS

TOTAL FOR ALL FILES
L97             8 (L3 OR L25) AND L13 AND L81

=> s l97 not (l76 or l40 or l18)
L98             0 FILE MEDLINE
L99             0 FILE BIOSIS
L100            0 FILE EMBASE
L101            0 FILE CAPLUS

TOTAL FOR ALL FILES
L102            0 L97 NOT (L76 OR L40 OR L18)

=> dis his ful

     (FILE 'HOME' ENTERED AT 15:51:29 ON 16 AUG 2007)

     FILE 'REGISTRY' ENTERED AT 15:51:38 ON 16 AUG 2007
L1                STR
L*** DEL2241598 S L
L2              5 SEA SSS SAM L1
L3            115 SEA SSS FUL L1
                  D L3 QUE STAT

     FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 15:53:18 ON 16 AUG 2007
L4              0 SEA ABB=ON  PLU=ON  L3
L5             23 SEA ABB=ON  PLU=ON  L3
L6              0 SEA ABB=ON  PLU=ON  L3
L7             41 SEA ABB=ON  PLU=ON  L3
     TOTAL FOR ALL FILES
L8             64 SEA ABB=ON  PLU=ON  L3
L9         115250 SEA ABB=ON  PLU=ON  CEREBR? VASCUL? DISEASE OR STROKE OR
                  CEREBROVASOSPASM OR BLOOD(5A)SUBARACHNOID OR HEAD INJUR?
L10         92093 SEA ABB=ON  PLU=ON  CEREBR? VASCUL? DISEASE OR STROKE OR
                  CEREBROVASOSPASM OR BLOOD(5A)SUBARACHNOID OR HEAD INJUR?
L11        125191 SEA ABB=ON  PLU=ON  CEREBR? VASCUL? DISEASE OR STROKE OR
                  CEREBROVASOSPASM OR BLOOD(5A)SUBARACHNOID OR HEAD INJUR?
L12         37304 SEA ABB=ON  PLU=ON  CEREBR? VASCUL? DISEASE OR STROKE OR
                  CEREBROVASOSPASM OR BLOOD(5A)SUBARACHNOID OR HEAD INJUR?
     TOTAL FOR ALL FILES
L13        369838 SEA ABB=ON  PLU=ON  CEREBR? VASCUL? DISEASE OR STROKE OR
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                CEREBROVASOSPASM OR BLOOD(5A) SUBARACHNOID OR HEAD INJUR?
L14           0 SEA ABB=ON  PLU=ON  L4 AND L9
L15           1 SEA ABB=ON  PLU=ON  L5 AND L10
L16           0 SEA ABB=ON  PLU=ON  L6 AND L11
L17           3 SEA ABB=ON  PLU=ON  L7 AND L12
     TOTAL FOR ALL FILES
L18           4 SEA ABB=ON  PLU=ON  L8 AND L13
L19           3 DUP REM L18 (1 DUPLICATE REMOVED)
                D 1-3 IBIB ABS HITSTR

     FILE 'REGISTRY' ENTERED AT 15:55:17 ON 16 AUG 2007
                E "N-HYDROXY-N'-(4-BUTYL-2-METHYLPHENYL)-FORMAMIDINE"/CN
                E HET0016/CN 5

     FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, WPIDS' ENTERED AT 15:56:21 ON 16
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L20          31 SEA ABB=ON  PLU=ON  "N-HYDROXY-N'-(4-BUTYL-2-METHYLPHENYL)-FORM
                AMIDINE" OR HYDROXY(L)BUTYL(L)METHYLPHENYL(L)FORMAMIDINE? OR
                HET0016
L21          45 SEA ABB=ON  PLU=ON  "N-HYDROXY-N'-(4-BUTYL-2-METHYLPHENYL)-FORM
                AMIDINE" OR HYDROXY(L)BUTYL(L)METHYLPHENYL(L)FORMAMIDINE? OR
                HET0016
L22          31 SEA ABB=ON  PLU=ON  "N-HYDROXY-N'-(4-BUTYL-2-METHYLPHENYL)-FORM
                AMIDINE" OR HYDROXY(L)BUTYL(L)METHYLPHENYL(L)FORMAMIDINE? OR
                HET0016
L23          28 SEA ABB=ON  PLU=ON  "N-HYDROXY-N'-(4-BUTYL-2-METHYLPHENYL)-FORM
                AMIDINE" OR HYDROXY(L)BUTYL(L)METHYLPHENYL(L)FORMAMIDINE? OR
                HET0016
L24           9 SEA ABB=ON  PLU=ON  "N-HYDROXY-N'-(4-BUTYL-2-METHYLPHENYL)-FORM
                AMIDINE" OR HYDROXY(L)BUTYL(L)METHYLPHENYL(L)FORMAMIDINE? OR
                HET0016
     TOTAL FOR ALL FILES
L25         144 SEA ABB=ON  PLU=ON  "N-HYDROXY-N'-(4-BUTYL-2-METHYLPHENYL)-FORM
                AMIDINE" OR HYDROXY(L) BUTYL(L) METHYLPHENYL(L) FORMAMIDINE?
                OR HET0016
L26           3 SEA ABB=ON  PLU=ON  L20 AND L9
L27           3 SEA ABB=ON  PLU=ON  L21 AND L10
L28           3 SEA ABB=ON  PLU=ON  L22 AND L11
L29           3 SEA ABB=ON  PLU=ON  L23 AND L12
L30           1 SEA ABB=ON  PLU=ON  L24 AND L13
     TOTAL FOR ALL FILES
L31          13 SEA ABB=ON  PLU=ON  L25 AND L13
L32           3 SEA ABB=ON  PLU=ON  L26 NOT L14
L33           2 SEA ABB=ON  PLU=ON  L27 NOT L15
L34           3 SEA ABB=ON  PLU=ON  L28 NOT L16
L35           0 SEA ABB=ON  PLU=ON  L29 NOT L17

     FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 15:57:46 ON 16 AUG 2007
L36           3 SEA ABB=ON  PLU=ON  L26 NOT L14
L37           2 SEA ABB=ON  PLU=ON  L27 NOT L15
L38           3 SEA ABB=ON  PLU=ON  L28 NOT L16
L39           0 SEA ABB=ON  PLU=ON  L29 NOT L17
     TOTAL FOR ALL FILES
L40           8 SEA ABB=ON  PLU=ON  L31 NOT L18
L41           4 DUP REM L40 (4 DUPLICATES REMOVED)
                D 1-4 IBIB ABS
L42         474 SEA ABB=ON  PLU=ON  ROMAN R?/AU
L43         752 SEA ABB=ON  PLU=ON  ROMAN R?/AU
L44         491 SEA ABB=ON  PLU=ON  ROMAN R?/AU
L45         544 SEA ABB=ON  PLU=ON  ROMAN R?/AU
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     TOTAL FOR ALL FILES
L46        2261 SEA ABB=ON  PLU=ON  ROMAN R?/AU
L47         334 SEA ABB=ON  PLU=ON  HARDER D?/AU
L48         596 SEA ABB=ON  PLU=ON  HARDER D?/AU
L49         323 SEA ABB=ON  PLU=ON  HARDER D?/AU
L50         262 SEA ABB=ON  PLU=ON  HARDER D?/AU
     TOTAL FOR ALL FILES
L51        1515 SEA ABB=ON  PLU=ON  HARDER D?/AU
L52         286 SEA ABB=ON  PLU=ON  MIYATA N?/AU
L53         354 SEA ABB=ON  PLU=ON  MIYATA N?/AU
L54         312 SEA ABB=ON  PLU=ON  MIYATA N?/AU
L55         848 SEA ABB=ON  PLU=ON  MIYATA N?/AU
     TOTAL FOR ALL FILES
L56        1800 SEA ABB=ON  PLU=ON  MIYATA N?/AU
L57        5522 SEA ABB=ON  PLU=ON  SATO M?/AU
L58        6740 SEA ABB=ON  PLU=ON  SATO M?/AU
L59        4543 SEA ABB=ON  PLU=ON  SATO M?/AU
L60       18124 SEA ABB=ON  PLU=ON  SATO M?/AU
     TOTAL FOR ALL FILES
L61       34929 SEA ABB=ON  PLU=ON  SATO M?/AU
L62          28 SEA ABB=ON  PLU=ON  KAMEO K?/AU
L63          55 SEA ABB=ON  PLU=ON  KAMEO K?/AU
L64          28 SEA ABB=ON  PLU=ON  KAMEO K?/AU
L65         131 SEA ABB=ON  PLU=ON  KAMEO K?/AU
     TOTAL FOR ALL FILES
L66         242 SEA ABB=ON  PLU=ON  KAMEO K?/AU
L67         390 SEA ABB=ON  PLU=ON  OKUYAMA S?/AU
L68         558 SEA ABB=ON  PLU=ON  OKUYAMA S?/AU
L69         345 SEA ABB=ON  PLU=ON  OKUYAMA S?/AU
L70         649 SEA ABB=ON  PLU=ON  OKUYAMA S?/AU
     TOTAL FOR ALL FILES
L71        1942 SEA ABB=ON  PLU=ON  OKUYAMA S?/AU
L72           0 SEA ABB=ON  PLU=ON  L42 AND L47 AND L52 AND L57 AND L62 AND
                L67
L73           0 SEA ABB=ON  PLU=ON  L43 AND L48 AND L53 AND L58 AND L63 AND
                L68
L74           0 SEA ABB=ON  PLU=ON  L44 AND L49 AND L54 AND L59 AND L64 AND
                L69
L75           1 SEA ABB=ON  PLU=ON  L45 AND L50 AND L55 AND L60 AND L65 AND
                L70
     TOTAL FOR ALL FILES
L76           1 SEA ABB=ON  PLU=ON  L46 AND L51 AND L56 AND L61 AND L66 AND
                L71
                D IBIB ABS
L77        6950 SEA ABB=ON  PLU=ON  (L42 OR L47 OR L52 OR L57 OR L62 OR L67)
L78        8888 SEA ABB=ON  PLU=ON  (L43 OR L48 OR L53 OR L58 OR L63 OR L68)
L79        5964 SEA ABB=ON  PLU=ON  (L44 OR L49 OR L54 OR L59 OR L64 OR L69)
L80       20447 SEA ABB=ON  PLU=ON  (L45 OR L50 OR L55 OR L60 OR L65 OR L70)
     TOTAL FOR ALL FILES
L81       42249 SEA ABB=ON  PLU=ON  (L46 OR L51 OR L56 OR L61 OR L66 OR L71)
L82          95 SEA ABB=ON  PLU=ON  (L3 OR L20 OR L9 ) AND L77
L83         108 SEA ABB=ON  PLU=ON  (L3 OR L21 OR L10) AND L78
L84          90 SEA ABB=ON  PLU=ON  (L3 OR L22 OR L11) AND L79
L85          57 SEA ABB=ON  PLU=ON  (L3 OR L23 OR L12) AND L80
     TOTAL FOR ALL FILES
L86         350 SEA ABB=ON  PLU=ON  (L3 OR L25 OR L13) AND L81
L87          93 SEA ABB=ON  PLU=ON  L82 NOT (L72 OR L36 OR L14)
L88         106 SEA ABB=ON  PLU=ON  L83 NOT (L73 OR L37 OR L15)
L89          88 SEA ABB=ON  PLU=ON  L84 NOT (L74 OR L38 OR L16)
L90          55 SEA ABB=ON  PLU=ON  L85 NOT (L75 OR L39 OR L17)
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     TOTAL FOR ALL FILES
L91          342 SEA ABB=ON  PLU=ON  L86 NOT (L76 OR L40 OR L18)
L92          186 DUP REM L91 (156 DUPLICATES REMOVED)
                 D 1 ABS
L93            2 SEA ABB=ON  PLU=ON  (L3 OR L20) AND L9 AND L77
L94            2 SEA ABB=ON  PLU=ON  (L3 OR L21) AND L10 AND L78
L95            2 SEA ABB=ON  PLU=ON  (L3 OR L22) AND L11 AND L79
L96            2 SEA ABB=ON  PLU=ON  (L3 OR L23) AND L12 AND L80
     TOTAL FOR ALL FILES
L97            8 SEA ABB=ON  PLU=ON  (L3 OR L25) AND L13 AND L81
L98            0 SEA ABB=ON  PLU=ON  L93 NOT (L72 OR L36 OR L14)
L99            0 SEA ABB=ON  PLU=ON  L94 NOT (L73 OR L37 OR L15)
L100           0 SEA ABB=ON  PLU=ON  L95 NOT (L74 OR L38 OR L16)
L101           0 SEA ABB=ON  PLU=ON  L96 NOT (L75 OR L39 OR L17)
     TOTAL FOR ALL FILES
L102           0 SEA ABB=ON  PLU=ON  L97 NOT (L76 OR L40 OR L18)


=> d l3 que stat
L1                STR
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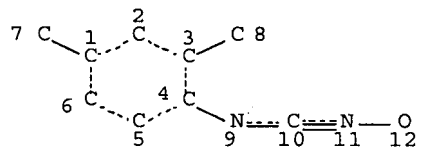


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED     187 ITERATIONS                          115 ANSWERS
SEARCH TIME: 00.00.01


=> log y

STN INTERNATIONAL LOGOFF AT 16:03:45 ON 16 AUG 2007
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